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The role of 3D imaging in the follow-up of patients with repaired tetralogy of Fallot

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Abstract. – OBJECTIVE: The patients with repaired Tetralogy of Fallot (rToF) are a growing population due to the improvement of surgical management in neonatal age. However, the significant pulmonary regurgitation, consequent to the repair, is the most frequent sequelae and leads to a progressive right ventricle dilation over time. The latter, in turn, is responsible for the possible dysfunction of right and/or left ventricle and an increased risk of dangerous ventricular arrhythmias. Therefore, right ventricle monitoring is necessary for rToF patients and a 3D method is required due to its three anatomical and functional subunits. Magnetic resonance imaging (MRI) has become the 3D modality of choice in the evaluation of both cardiac anatomy and ventricular volumes in rToF patients since it is able to evaluate both the pathophysiology and anatomy, it is free of radiation and, when strictly necessary, it uses a non-iodinated contrast agent. Cardiac CT should be considered in the evaluation of the sequelae in rToF only in selected cases, given that it implies a radiation dose and iodinated contrast, in addition to not evaluating the pathophysiology as MRI.

Key Words
MRI, Tetralogy of Fallot, Cardiac CT, Right ventricle, Pulmonary arteries, Right outflow tract.

Abbreviations

ToF: Tetralogy of Fallot; RV: Right ventricle; CT: Computed tomography; MRI: Magnetic resonance imaging; CHD: Congenital heart disease; rToF: Repaired Tetralogy of Fallot; 3D: Three-dimensional; RVOT: Right ventri-cle outflow tract; LGE: Late gadolinium enhancement; PVR: Pulmonary valve replacement; LV: Left ventricle; SSFP: Steady-state free precession; PC: Phase-contrast; PT: Pulmonary trunk; CNR: Contrast-to-noise ratio; TSE: Turbo spin echo; CE-MRA: Contrast-enhanced 3D magnetic resonance angiography; ECV: Myocardial extracellular volume; WSS: Wall shear stress; LPA: Left pulmonary artery; MPA: Main pulmonary artery; CAD: Computed-aided design

Introduction

Tetralogy of Fallot (ToF) is the most common cyanotic congenital heart disease (CHD) with an incidence of approximately 1/3600 live births, accounting for 5-7% of all CHD[1]. Surgical correction involves closing the ventricular septal defect and broadening the pulmonary outflow tract. As the surgical treatment of ToF has evolved considerably since the first systemic artery to pulmonary shunt of Blalock-Taussig, early surgical mortality also decreased from 50% in the late 1950s to less than 2% recently[2]. Timing and the type of surgical technique and its effect on the long-term prognosis are determined by the level of the obstruction of the pulmonary outflow tract and the patient's clinical conditions[3]. With the improvement of surgical techniques, the long-term prognosis of ToF has been modified, increasing the number of adults with repaired ToF (rToF), who are now more than those under 18 years of age[4]. Therefore, regular and detailed imaging evaluation of patients with ToF during follow-up is fundamental to prevent long and mid-term adverse clinical outcomes[5]. Transthoracic echocardiography is the first line of cardiovascular imaging modality, especially for young infants, providing a good assessment of the pre and postoperative cardiac anatomy. However, this method has its limitations due to the poor acoustic window and technical limitations in the evaluation of three-dimensional (3D) right ventricular shape[6]. Owing to variable ultrasound tissue interaction, the image resolution of conventional two-dimensional techniques is not adequate to an accurate evaluation of all three anatomical and functional subunits of the right ventricle (the inlet, the apical trabecular and the outlet, also called infundibulum). It is fundamental to assess accurately the right ventricular volume and function along with the integrity of the right ventricular outflow tract and the pulmonary arteries in rToF patients.

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Therefore, in the 3D evaluation of both cardiac anatomy and ventricular volumes in rToF patients, the use of other imaging modalities, such as magnetic resonance imaging (MRI) and computed tomography (CT), is mandatory. Cardiac catheterization nowadays is rarely undertaken, except only to estimate right ventricular pressure and perform interventional procedures. The goal of this review is to elucidate the information obtained from CT and/or MRI, useful in the clinical follow-up of rToF patients, with attention in deciding timing and type of pulmonary valve replacement. The decision to use the best non-invasive imaging in consideration of the age interval and the clinical-diagnostic approach represents a unique challenge for cardiologists and radiologists, for a patient-specific evaluation.

Anatomical Description

Tetralogy of Fallot often consists in an association of obstruction of the pulmonary outflow tract, an overriding aorta, a ventricular septal defect due to misalignment and right ventricular hypertrophy. Stenosis of the infundibulum is an integral part of the condition and has a dynamic component. The pulmonary valve can display a broad spectrum of abnormalities, ranging from mild to severe obstruction of the right ventricle outflow tract (RVOT) up to pulmonary valve atresia. Finally, pulmonary branches can also present various degrees of stenosis/hypoplasia at different levels.

Surgical Approach

The timing and type of first surgery, follow-up and pulmonary valve replacement depend on the level of pulmonary outflow tract obstruction and the degree of stenosis/hypoplasia of pulmonary arteries. In addition to the above variables, the abnormalities often associated with ToF, such as coronary artery abnormalities or atrioventricular septal defects should be considered.

The surgical correction involves closing the ventricular septal defect and broadening the pulmonary outflow tract using a trans-annular or infundibular patch with pulmonary valvuloplasty. In the presence of coronary artery abnormalities, a conduit between the right ventricle and the pulmonary arteries (RV-PA conduit) might be required. A palliative procedure (e.g., a modified Blalock-Taussig shunt which involves inserting a 3.5 to 5 mm prosthetic tube between the brachiocephalic trunk or subclavian artery and the ipsilateral pulmonary artery) is needed in patients with severely hypoplastic pulmonary arteries.

Postoperative Sequelae and Residual Lesions

The most common late postoperative sequelae and residual lesions include pulmonary regurgitation, right ventricular dilation and failure, residual main and branch pulmonary artery stenosis, tricuspid regurgitation, right ventricular outflow tract aneurysm and dyskinesis, conduit failure, left pulmonary artery kinking and residual or recurrent ventricular septal defect.

Imaging: MRI or CT?

MRI has been recognized as a more reliable tool, because of its independence from the acoustic window, lack of ionizing radiation, non-invasive 2D and 3D evaluation of right ventricle and great vessel, as well as its reproducibility in the longitudinal follow-up of rToF patients[7-9]. MRI is the only modality able to elucidate both the morphology and pathophysiology of congenital heart diseases[6]. In rToF patients, it allows the quantitative and qualitative assessment of the three RV-portions, including the most accurate measurement of RV volume that is often increased in these patients due to significant chronic pulmonary regurgitation[10]. With this method it is possible to achieve a good intra- and interobserver reproducibility of right ventricle size and function measurements[11]. In addition, MRI provides useful information on the regional RV function, having the unique possibility to compare a regional dysfunction, for example an akinetic region due to the patch, with the presence of scars by using LGE[12]. Moreover, it offers a more accurate method for the noninvasive quantification of blood flow in rToF, useful to quantify pulmonary regurgitation, differential pulmonary branches blood flow, the magnitude of cardiac shunts and pressure gradients across narrow segments[13]. Finally, MRI allows the three-dimensional evaluation of thoracic vessel anatomy (pulmonary trunk, pulmonary artery branches, aorta) using different sequences, some of which not requiring the administration of contrast agents differently from CT (such as 3D SSFP navigator and 3D TSE)[14-16]. On the other hand, CT is preferred to MRI to obtain anatomical information of the tracheobronchial tree, owing to its higher spatial resolution or in case of endovascular stents or stent-mounted valves, for its independence from metallic artifacts[17]. Furthermore, CT is preferred when a fast excellent anatomical evaluation of the heart in infants and non-collaborative children is required, especially to assess the course of the coronary arteries. The new dual-source mul-

tidetector CT scanners[18,19] can take an image of the chest in less than 1 sec, eliminating the need for a breath-hold in infants and children, as well as sedation, with a small radiation dose delivered. On the contrary, despite all its advantages and technological advances, MRI requires a long scan time and a perfect breath hold collaboration for the majority of the images acquired, needing general anesthesia in infants and young children. In addition, even though CT has less temporal resolution than MRI[20], it should be taken into consideration for the assessment of the ventricular volume and function in the presence of PMK/ICD or claustrophobia. To sum up, CT use is restricted to a few selected cases, since its usage implies a certain radiation dose and potentially dangerous reactions to iodinated contrast agents, so harmful in young pediatric populations. In synthesis, MRI is used in rToF patients to:

1. Assess quantitatively right and left ventricle volumes, mass, stroke volumes and ejection fraction;
2. Evaluate regional wall motion abnormalities;
3. Image the anatomy of the right ventricle outflow tract, pulmonary arteries and aorta;
4. Quantify atrioventricular and semilunar valve regurgitation, cardiac output, and pulmonary-to-systemic flow ratio;
5. Assess myocardial viability (LGE);
6. Visualize coronary artery anatomy.

CT can be alternatively used:

1. When MRI is contraindicated (i.e., claustrophobia, PMK/ICD) for the anatomy (intra- and extra-cardiac, coronaries), right and left ventricle volumes and ejection fraction and tracheobronchial tree;
2. In the presence of stent or prosthetic valve or alleged paravalvular leak for the anatomy;
3. In infants and non-collaborative children for the anatomy and the tracheobronchial tree.

MRI Applications Overview in rToF Patients: Cine-Images

Steady-state free precession (SSFP) cine images are the most useful sequences for qualitative and quantitative assessment of the biventricular size and function[21] in right ventricular dilation and dysfunction of rToF patients[22]. Indeed, chronic pulmonary valve regurgitation, the most common cardiovascular sequelae in rToF, progressively leads to right ventricular enlargement (Figure 1) and dysfunction, ventricular arrhythmias, heart failure and death[23]. MRI has proven

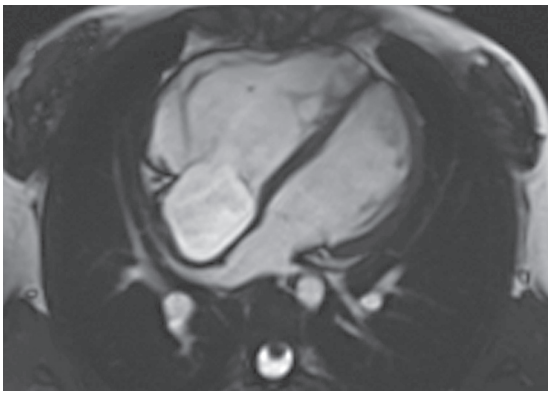

Figure 1. Right ventricular dilation on 4-chambers view (SSFP cine sequence).

to be suitable for accurate and reproducible measurement of ventricular size and function[11,24], fundamental in these patients to monitor RV dilation over time. Pulmonary valve replacement (PVR) in asymptomatic rToF patients is based mainly on the RV size and function[25]. Therefore, the proper documentation of how RV volume dilates over time in this cardiac disease is fundamental to choose the PVR exact timing before right/left ventricle dysfunction and/or ventricular arrhythmias onset. Knauth et al[26] found that severe RV dilation (end-diastolic volume Z-score ≥7 measured by MRI) and ventricular dysfunction (LV EF <55% or RV <45%) are independent predictors of late adverse outcomes (death, sustained ventricular tachycardia, heart failure) late after rToF. However, in the majority of rToF patients, clinical status is not a reliable marker of changes in RV dilation and/or function. Therefore, researchers have attempted to establish a threshold of RV end-diastolic volume below which postoperative normalization of RV size and−function can be expected[27,28]. Cut-off values for indexed RV end-diastolic and systolic volume, respectively between 150 and 170 ml/m^2 and 80 and 90 ml/m2, have been proposed as an indication for PVR in asymptomatic patients with rToF[27-32]. This year, the AHA/ACC guideline for the management of adults with congenital heart disease suggests taking into consideration any 2 of the following MRI parameters: mild or moderate RV or LV systolic dysfunction (RV EF <47% or LV EF <55%), severe RV dilation (RVEDVI ≥160 mL/m^2, or RVESVI ≥80 mL/m^2, or RVEDV ≥2 x LVEDV), right ventricle systolic pressure due to RVOT obstruction ≥2/3 systemic pressure[33-34].

The main problem in this disease is that RV dilation over time seems to differ from patient to patient, even in the presence of the same hemodynamically significant pulmonary regurgitation[35] as well as the threshold of RV dilatation at which the right dysfunction can begin and the risk of arrhythmias increases. MRI longitudinal studies have pointed out that, in the majority of patients, RV growth seems to be very slow over time. Only 15% of rToF patients seem to develop a worse and faster RV dilatation, as reported by Wald et al[36]. However, considering that we do not know yet in which rToF patients this may occur, all of them should undergo seriated MRI examinations (every 2 or 3 years) to monitor the right ventricular dilation and prevent its subsequent dysfunction.

SSFP cine images can also perfectly assess the estimated position of the patch on the right ventricle, because this area appears as an akinetic region, due to the absence of contraction during the cardiac cycle[37].

Moreover, SSFP cine sequence can evaluate, in case of residual/recurrent RVOT obstruction, the narrowing with resultant turbulent flow jet at the stenosis level (Figure 2), as well as the hypoplasia/stenosis of pulmonary arteries. However, especially in case of RVOT obstruction, the turbulent flow jet can reduce image quality, requiring an additional sequence, such as gradient echo sequence. The latter, being less sensitive to turbulence artifacts, allows visualizing the anatomy of RVOT obstruction in 2D cine better than SSFP ones.

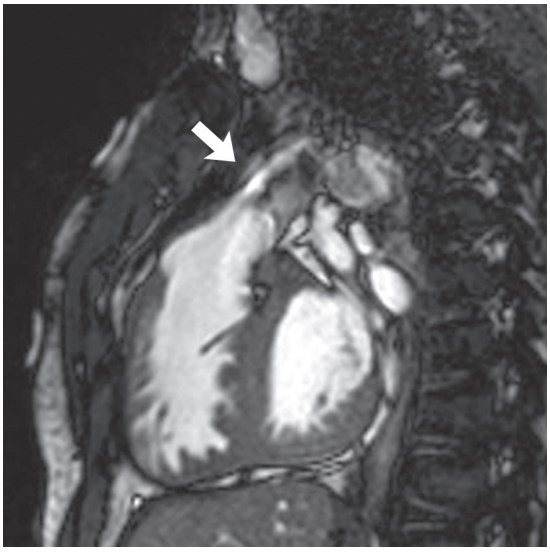

Figure 2. Turbulent flow jet at the level of the stenosis on sagittal view (SSFP cine sequence).

Phase Contrast MR Imaging for Blood Flow Quantification in Valves and Pulmonary Arteries

Phase-contrast (PC) sequence is useful to quantify regurgitant volumes of main vessels, such as the aorta and the pulmonary artery, to estimate the distribution of the flow to the pulmonary arteries and to quantify the severity of cardiac shunts. The principal pitfall is to set the sequence using a proper velocity-encoding rate to avoid aliasing artifacts. MRI is the most accurate and reproducible method for quantification of pulmonary regurgitation[13]. In addition, PC MRI imaging in rToF patients can be used for the assessment of the pressure gradient through a residual right ventricle outflow tract (RVOT) stenosis[29,38]. Finally, it allows a direct quantification of blood flow in the pulmonary branches, which is crucial for determining the hemodynamic significance of a stenosis. The normal flow distribution is 55% in the right pulmonary artery and 45% in the left pulmonary one.

3D Anatomy Evaluation

Cardiac MRI enables the three-dimensional evaluation of thoracic vessel anatomy in rToF patients (pulmonary trunk, pulmonary artery branches, aorta, aorta-pulmonary collaterals) by using four types of sequences (3D SSFP navigator, 3D TSE, CE-MRA, gated CE-MRA). The first two sequences do not require a contrast agent, on the contrary of the second two.

3D SSFP navigator sequence is easy to perform and does not require contrast administration and breath hold collaboration, preserving the accuracy of dimensions, since it is set both with the breathing and the ECG of the patient[16,39,40]. Using a prospective breathing-trigger that allows the acquisition of the signal only at a given phase of the respiratory cycle when the "time-windows" of the two gating (cardiac and respiratory) are combined, it significantly reduces breathing artifacts, only requiring patients to be still. Furthermore, this sequence can be set at the required phase of the cardiac cycle in relation to the clinical issue, useful in congenital heart disease. Set in rToF patients at mid-diastole, it is used to assess the origin and the proximal course of coronaries. Finally, at end-systole, this sequence allows to take the dimensions of the PT at three levels (pulmonary valve remnant, mid-portion, bifurcation), when the pulmonary trunk (PT) is at its maximum expansion. This assists the clinician in the choice of the options available for PVR (surgery or interventional procedure) (Figure 3). Lately,

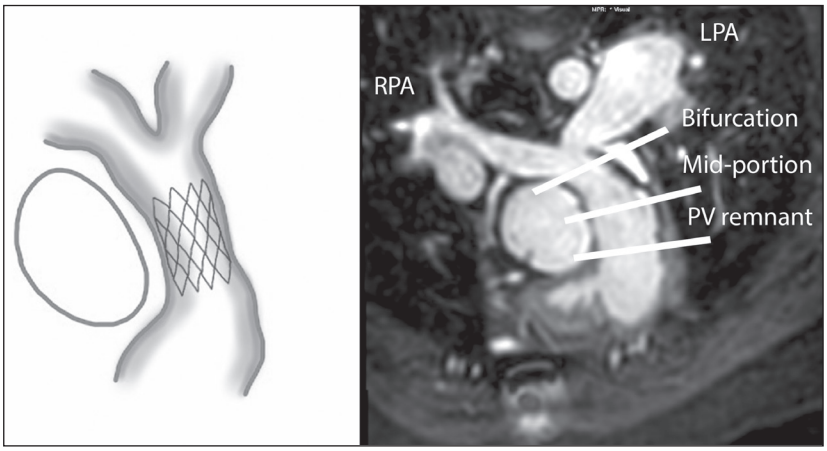

Figure 3. The figure shows: on the left where the hybrid stent, and successively the covered CP stent and prosthetic valve, are implanted in right ventricle outflow tract; on the right where the measurements are taken in the 3D SSFP navigator sequence. RPA = Right Pulmonary Artery; LPA = Left Pulmonary Artery; PV = Pulmonary valve.

this sequence has been preferred to CE-MRA and gated CE-MRA in taking the dimensions of the vessels, such as pulmonary arteries, aorta, etc.[16,41], thanks to its many advantages (versatility, facility of execution, dimension accuracy, contrast-free). The main drawback of the 3D SSFP navigator sequence is the susceptibility to the artifacts from cardiac stents and metallic valve prostheses, besides the prolonged acquisition time.

The 3D T1 turbo spin echo (TSE) sequence, with cardiac and respiratory gating, compared to 3D SSFP navigator, goes beyond the problem of artifacts in patients with stents in the pulmonary arteries and/or in the right ventricular outflow, as well as in rToF who underwent PVR (Figure 4). Spin-echo based imaging techniques are known to be less sensitive to metallic artifacts than SSFP and CE-MRA sequences. The 3D TSE sequence is helpful in the delineation of larger anatomical structures, while evaluation of small coronary arteries is problematic due to the small vessel size. In addition, it takes a role in the measurements of vessels containing implanted stent, even if the dimensions could be larger than those obtained with CE-MRA, although Malayeri et al[14] found this difference not statistically significant. Recently, this sequence, commercially known as SPACE, has been compared to cardiac CT[42]. It has helped obtain luminal measurements, which correlate well with cardiac CT only with a little overestimation, without the necessity of ionizing radiations and contrast administration. SPACE sequence can also be set at end-systole, being useful to take PT measurements at its maximum expansion. Finally, it may provide the evaluation of the tracheobronchial tree, although CT has a higher spatial resolution. The potential pitfall of 3D turbo spin echo sequence, as well as 3D SSFP navigator, includes prolonged acquisition time, which might be a hindrance, especially in patients who undergo general anesthesia for MRI scans and in children. Contrast-enhanced 3D magnetic resonance angiography (CE-MRA) is a fast imaging technique able to evaluate large arteries and veins. This sequence is comparable to catheterization in the evaluation of pulmonary branches and major vessels, but it is non-invasive, uses safe contrast agents and, more importantly, is free of ionizing radiations[43]. It does not require ECG triggering given that it is a fast 3D spoiled gradient echo and it can be performed within a breath-hold length (less than 25 s) to suppress bulk breathing motion. However, despite being unaffected by arrhythmias, there could be a certain degree of blurring, caused by ecg-triggering absence, in the delineation of the

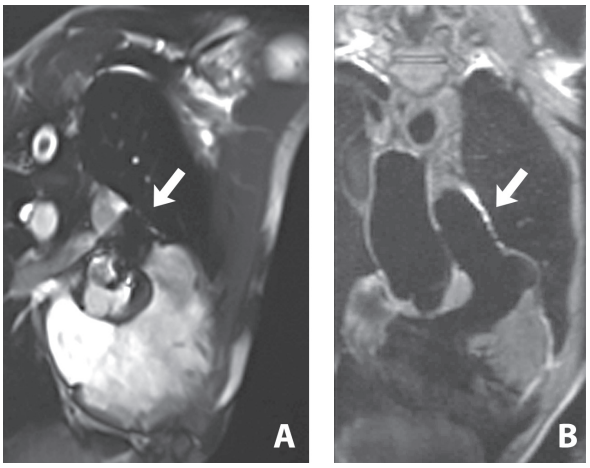

Figure 4. A, Artifacts on RVOT due to a prosthetic valve in SSFP cine image. **B**, The same image in 3D TSE sequence without artifacts with a good delineation of the anatomy.

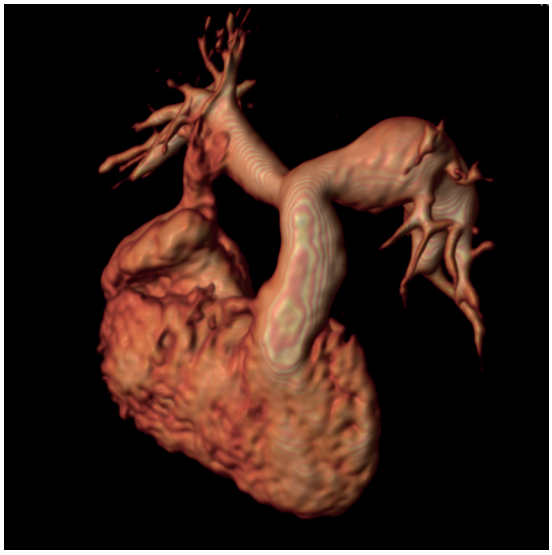

Figure 5. 3D view of the RVOT and pulmonary arteries by volume rendering using MRI.

ventricular outflow vessels. In conclusion, conventional CE-MRA is sensitive to cardiac and respiratory motion artifacts and it cannot be set at a specific phase acquisition of the cardiac cycle. Thus, the vessel measurements could be under or overestimated, as well as influenced by the blurred image. Although CE-MRA is an excellent sequence to obtain an overall 3D view of the RVOT and pulmonary arteries by multiplanar reformatting and volume rendering (Figure 5), it cannot be helpful when choosing between surgery and interventional procedure in PVR in rToF with patch transannular or infundibular correction. To address this limitation, recently CE-MRA has been acquired with ECG-gated, whereby the segmental data acquisition is synchronized with the cardiac cycle, leading to an improvement of the image sharpness[44]. Unfortunately, gated CE-MRA has the limitation to allow only a restricted anatomic coverage due to the acquisition of only a single 3D partition per heartbeat, precluding high spatial resolution imaging of the entire thorax[44]. In addition, it is challenging to obtain a perfect RVOT and pulmonary arteries imaging, because of the competing demands of high spatial resolution while imaging in a narrow window of the cardiac cycle within a breath-hold. Finally, also this sequence requires the use of a contrast agent (gadolinium), whose potential toxicity cannot be ignored.

Late Gadolinium Enhancement

The late gadolinium enhancement (LGE) technique has been recognized as a current clinical practice for the characterization of myocardial tissue in ischemic and non-ischemic cardiomyopathies. In rToF, LGE can identify myocardial scar due to the surgical scarring of the right ventricle and interventricular septum (Figure 6). Babu-Narayan et al[45] showed that 2D LGE in 92 rToF patients is commonly seen within RVOT and ventricular septal defect sites, but may also involve the inferior right ventricle insertion point and the left ventricle wall. In this study, the burden of RV scar was associated with impaired exercise capacity, RV systolic dysfunction, a worse clinical status (NYHA III-IV) and cardiac arrhythmias. Wald et al[12] demonstrated that a segmental surgical scar was correlated with a reduction of systolic function of RVOT and global RV, and subsequently to an increased prevalence of sustained ventricular tachycardia.

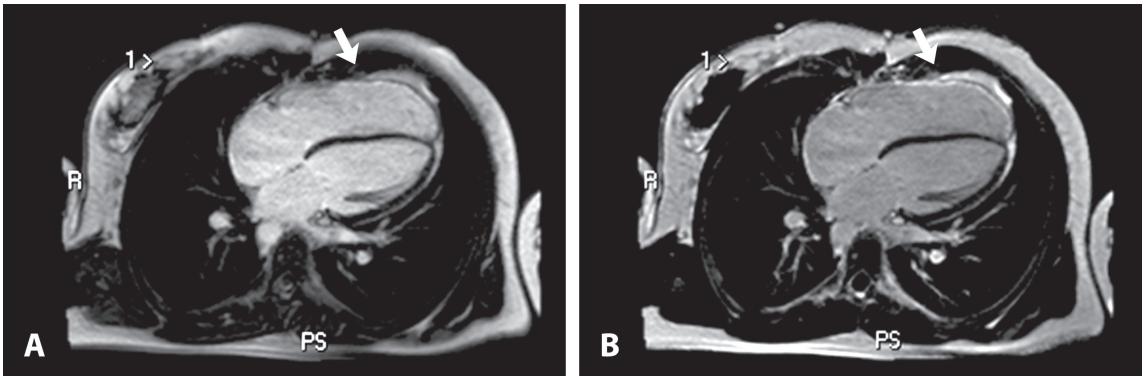

Figure 6. Late enhancement on 4-chambers view identifies scar on the free wall of the right ventricle: **A**, inversion recovery [IR] sequence; **B**, phase-sensitive inversion recovery [PSIR].

T1 Mapping

Recently, a new MRI technique, measuring the T1 relaxation times before and after administration of gadolinium contrast and using hematocrit value, evaluates the myocardial extracellular volume (ECV), an indirect measure of diffuse myocardial fibrosis[46]. Kozak et al[47] reported shorter post-contrast T1 times in the left ventricular lateral wall and the right ventricular anterior wall of rToF patients. In addition, they found that RV was more damaged than LV and the anterior wall of RV was more involved than the inferior segments[47]. Chen et al[48] demonstrated a positive correlation between the LV and RV ECV values and an association between RV ECV and volume overload in rToF patients. Moreover, they correlated the degree of fibrosis in both the ventricles with the patient's prognosis[48], identifying a LV ECV high value (above 28%) as an independent predictor of arrhythmias in this population. Non-invasive early detection of diffuse myocardial fibrosis could be useful to improve risk stratification and guide therapeutic interventions in rToF patients.

4D Flow Assessment

4D flow imaging is a new technique that allows a comprehensive evaluation of vascular hemodynamics, through a combined data acquisition of 3 spatial dimensions and 3 blood flow velocity directions during the cardiac cycle[49,50]. The 4D technique enables multiple vessels evaluation in a single acquisition, repositioning flow measurement planes during post-processing analysis[51]. 4D flow MRI studies have shown marked differences between rToF patients' RVOT and pulmonary artery flow features and those of volunteers[52,53].

François et al[53] reported that the right atrium and ventricle flow patterns in patients with rToF were different from those in normal volunteers, thus suggesting that hemodynamics alterations may precede morphological changes of the right ventricle. Finally, the 4D flow is able to analyze flow-related features and it permits the understanding of the interactions between pulmonary regurgitation, pulmonary artery stiffening and right heart function.

3D Models

MRI may provide 3D model computational analysis for the hemodynamic assessment of pulmonary artery and branches, useful to evaluate wall shear stress (WSS) and pressure distribution, which could help planning reconstructive surgery for complex congenital heart disease (CHD).

The branch pulmonary artery stenosis constitutes one of the most frequent postoperative complications in rToF[54]. In addition, the angulation between the left pulmonary artery (LPA) and main pulmonary artery (MPA) has emerged as a morphological risk factor for late clinical complications[54,55], affecting the pulmonary hemodynamics.

Finally, we correlated 3D RV shape with clinical parameters in patients with rToF using computer modeling[56], showing a relationship between the RV dilation (as the outlet bulges and the apex deforms) and PR volume worsening.

Strain Imaging

Regional myocardial strain, which is usually measured in 3 components, circumferential, longitudinal and radial strain, have the potential to identify myocardial dysfunction before depression of global measures of ventricular contractilities, such as ejection fraction. Ordovas et al[57] described how MR imaging tagging could aid in the early detection of left ventricular dysfunction in patients with pulmonary regurgitation after rToF. The authors showed that rToF patients have significantly decreased left ventricular peak circumferential strain at the base and apex levels compared with normal volunteers. Moreover, the left ventricular peak rotation at the basal and mid-ventricular levels was also delayed in these patients compared with volunteers. Additionally, the same investigators documented the association between abnormal ventricular septal excursion and reduced global and left ventricular systolic function. It also corresponded with the presence of fibrosis in the interventricular septum and at the right and left ventricular insertion points, thus suggesting that this technique may be able to identify adverse interventricular interactions. Finally, abnormalities in global myocardial strain have been found in obese rToF patients[58] compared to ones with appropriate weight, proposing again the severe health epidemic problem of obesity[59-62] even in children and adults with congenital heart disease.

Cardiac CT

Cardiac computed tomography (Cardiac CT) has the advantage to provide excellent spatial resolution in very rapid acquisition time, such as a single breath-hold. Furthermore, it allows the acquisition of thoracic or cardiac volume that can be reconstructed in multiple spatial planes.

In rToF patients, cardiac CT is used mainly for anatomical evaluation[63-65]. Indeed, cardiac CT has proven to be really useful for the evaluation of coronary artery course in case of coronary abnormalities, present in 9-12% of patients with ToF[66] (Figure 7). In particular, it is fundamental in assessing

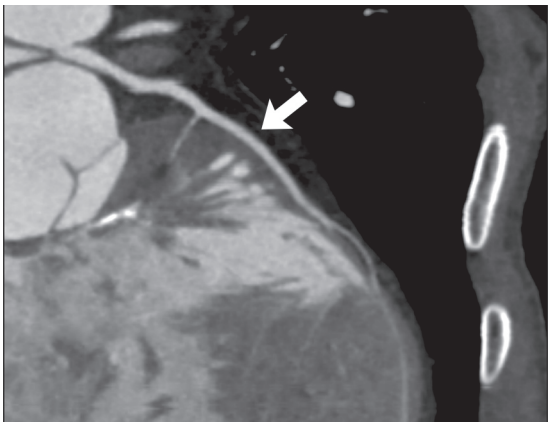

Figure 7. Left anterior descending artery on cardiac CT.

the relationship between the coronary arteries and RVOT to prevent any compression of the coronary arteries during PVR procedure. In addition, cardiac CT is preferred to MRI, when an anatomical evaluation of position and integrity of endovascular stents (Figure 8) or stent-mounted valves are required, or in the presence of a pseudoaneurysm formation or aneurysmal dilation of an RV-PA conduit.

In rToF patients with conduits, especially homograft, cardiac CT is capable of visualizing the tissue calcification (Figure 9), contrary to MRI. This information is essential to guide percutaneous pulmonary valve implantation in RV-PA conduits. In rToF patients with transannular patch, it can also identify the patch (Figure 10). Additionally, cardiac CT is fundamental in the complication of endocarditis, such as vegetations on the conduit, embolism of material from the vegetations, leaky valve, and abscesses around the valve. Finally, cardiac CT could be decisive in rare cases of fracture and/or dissection (Figure 11) or extended thrombosis of the conduit.

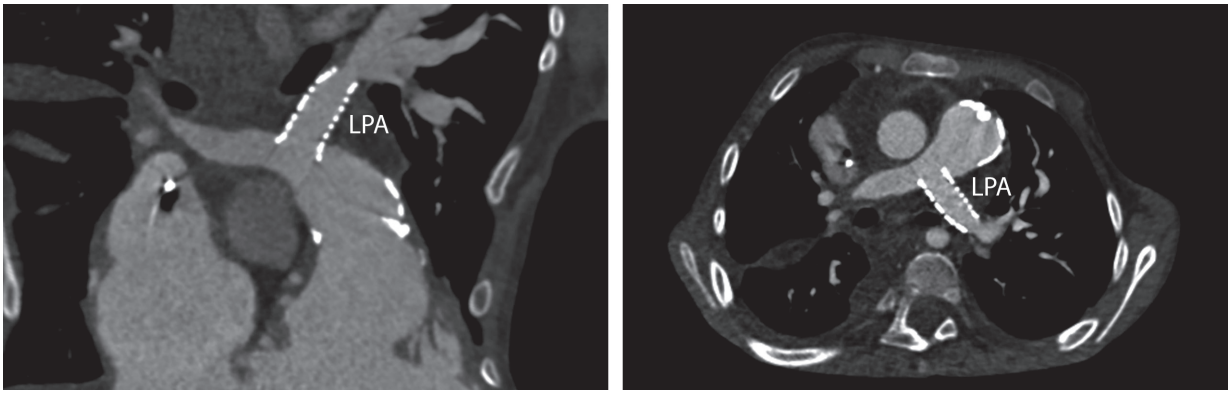

Figure 8. Stent on the right pulmonary artery visualized with cardiac CT.

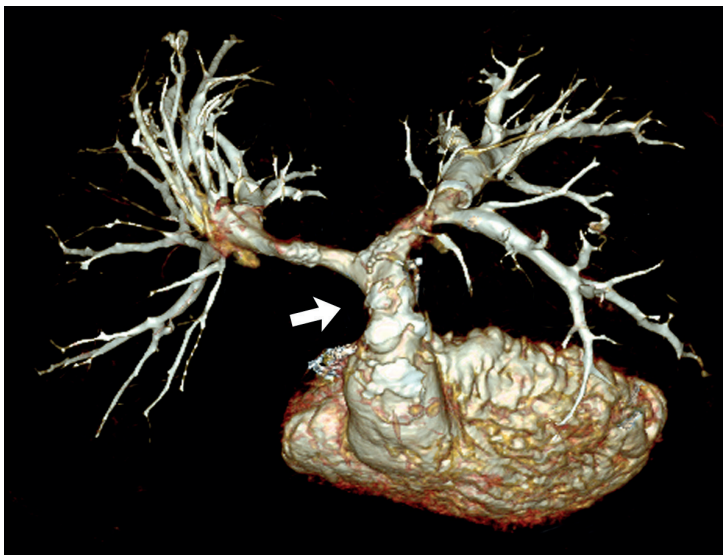

Figure 9. Calcium on the conduit visible with cardiac CT (3D volume rendering reconstruction).

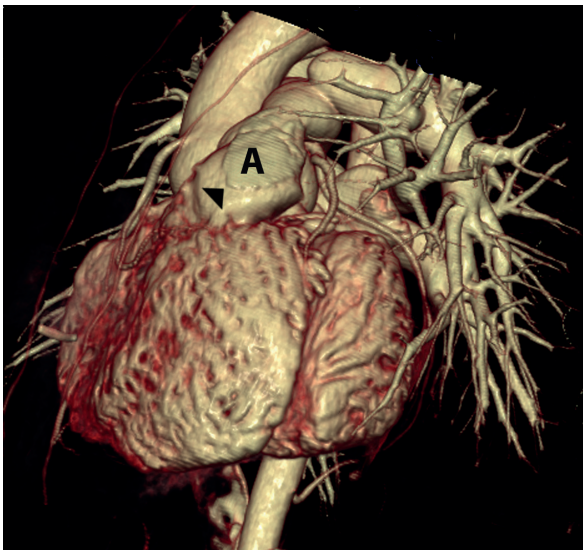

Figure 10. Patch A, on RVOT evaluated with cardiac CT (3D volume rendering reconstruction).

The anatomical evaluation by cardiac CT should be preferred to MRI, in a determined age range of the patient, as it does not require general anesthesia. The ionizing radiation foreseen by cardiac CT can be justified in children, only if it allows avoiding general anesthesia with orotracheal intubation and only the assessment of heart anatomy is required. In addition, the anatomical information can be achieved by using ECG-prospective acquisition, reducing the necessary dose of radiations. It should be added that the new dual source multi-detector CT scanners can image the thorax in less than 1 sec, eliminating the need for a breath-hold in infants and children and the radiation dose delivered is small, in case of anatomic evaluation[19,67].

In patients with PMK or other contraindications to MRI, cardiac CT also allows evaluating the biventricular volume and function[61], although it has a worse temporal resolution and requires a high radiation dose having to acquire for the whole cardiac cycle.

Undoubtedly, the size and function, by cardiac CT, can be assessed only using an ECG- retrospective acquisition, which requires a higher dose of ionizing radiation, compared to the ECG-prospective one, because the data acquisition covers the whole cardiac cycle. The retrospective acquisition is helpful also for the evaluation of kinesis abnormalities such as RVOT aneurysm. Finally, CT is preferred in rToF patients with airway involvement, due to its major spatial resolution.

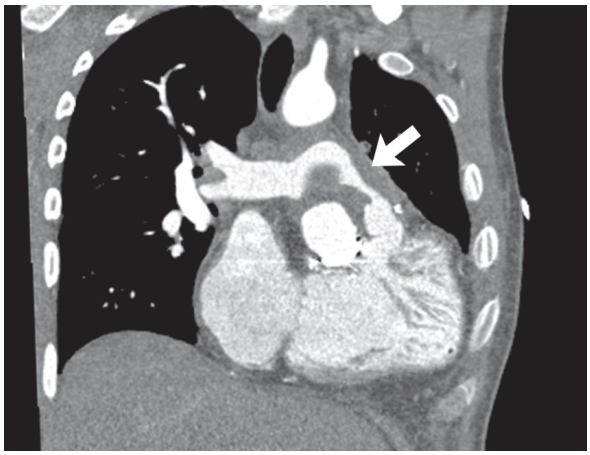

Figure 11. RV-PA conduit fracture and dissection on cardiac CT (3D multi-planar reconstruction). The conduit lumen is markedly reduced (displayed in white).

Conclusions

The pathophysiology of rToF is complex; so far, it is still unclear how the right ventricle can behave in each patient over time, probably because all factors involved in the RV progressive dilation and their exact role are still not perfectly known. However, during follow-up of rToF patients, a significant increase in ventricular dysfunction, exercise intolerance, heart failure symptoms, arrhythmias and death have been detected. Therefore, MRI should be an essential diagnostic tool in this growing patient population and it should be performed at regular intervals. In addition, maintaining consistency and reproducibility of measurements should be the goal of each MRI laboratory, given the importance of RV size and function in rToF patients to PVR timing. Finally, MRI is likely to continue to play a key role in research to improve the outcomes of rToF patients. CT should be performed only in selected cases.

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Conflict of Interests

The authors declare that they have no conflict of interest.

References

1) Apitz C, Webb GD, Redington AN. Tetralogy of Fallot. Lancet 2009; 374: 1462-1471.

2) Villafañe J, Feinstein JA, Jenkins KJ, Vincent RN, Walsh EP, Dubin AM, Geva T, Towbin JA, Cohen MS, Fraser C, Dearani J, Rosenthal D, Kaufman B, Graham TP. Adult congenital and pediatric cardiology section, American College of Cardiology. Hot topics in tetralogy of Fallot. J Am Coll Cardiol 2013; 62: 2155-2166.
3) Tretter JT, Friedberg MK, Wald RM, McElhinney DB. Defining and refining indications for transcatheter pulmonary valve replacement in patients with repaired tetralogy of Fallot: contributions from anatomical and functional imaging. Int J Cardiol 2016; 221: 916-925.
4) Nollert G, Fischlein T, Bouterwek S, Bohmer C, Klinner W, Reichart B. Long-term survival in patients with repair of tetralogy of Fallot: 36-year follow-up of 490 survivors of the first year after surgical repair. J Am Coll Cardiol 1997; 30: 1374-1383.
5) Vaujois L, Gorincour G, Alison M, Dery J, Poirier N, Lapierre C. Imaging of postoperative tetralogy of Fallot repair. Diagn Interv Imaging 2016; 97: 549-560.
6) Kilner PJ. The role of cardiovascular magnetic resonance in adults with congenital heart disease. Prog Cardiovasc Dis 2011; 54: 295-304.
7) Geva T. Is MRI the preferred method for evaluating right ventricular size and function in patients with congenital heart disease?: MRI is the preferred method for evaluating right ventricular size and function in patients with congenital heart disease. Circ Cardiovasc Imaging 2014; 7: 190-197.
8) Valente AM, Cook S, Festa P, Ko HH, Krishnamurthy R, Taylor AM, Warnes CA, Kreutzer J, Geva T. Multimodality imaging guidelines for patients with repaired tetralogy of Fallot: a report from the American Society of Echocardiography: developed in collaboration with the society for cardiovascular magnetic resonance and the Society for Pediatric Radiology. J Am Soc Echocardiogr 2014; 27: 111-141.
9) Geva T. Repaired tetralogy of Fallot: the roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support. J Cardiovasc Magn Reson 2011; 13: 9.
10) Buechel ER, Dave HH, Kellenberger CJ, Dodge-Khatami A, Pretre R, Berger F, Bauersfeld U. Remodelling of the right ventricle after early pulmonary valve replacement in children with repaired tetralogy of Fallot: assessment by cardiovascular magnetic resonance. Eur Heart J 2005; 26: 2721-2727.
11) Blalock SE, Banka P, Geva T, Powell AJ, Zhou J, Prakash A. Interstudy variability in cardiac magnetic resonance imaging measurements of ventricular volume, mass, and ejection fraction in repaired tetralogy of Fallot: a prospective observational study. J Magn Reson Imaging 2013; 38: 829-835.
12) Wald RM, Haber I, Wald R, Valente AM, Powell AJ, Geva T. Effects of regional dysfunction and late gadolinium enhancement on global right ventricular function and exercise capacity in patients with repaired tetralogy of Fallot. Circulation 2009; 119: 1370-1377.
13) Varaprasathan GA, Araoz PA, Higgins CB, Reddy GP. Quantification of flow dynamics in congenital heart disease: applications of velocity-encoded cine MR imaging. Radiographics 2002; 22: 895-905.
14) Malayeri AA, Spevak PJ, Zimmerman SL. Utility of a high-resolution 3D MRI sequence (3D-SPACE) for evaluation of congenital heart disease. Pediatr Cardiol 2015; 36: 1510-1514.
15) Fenchel M, Greil GF, Martirosian P, Kramer U, Schick F, Claussen CD, Sieverding L, Miller S. Three-dimensional morphological magnetic resonance imaging in infants and children with congenital heart disease. Pediatr Radiol 2006; 36: 1265-1272.
16) Francois CJ, Tuite D, Deshpande V, Jerecic R, Weale P, Carr JC. Unenhanced MR angiography of the thoracic aorta: initial clinical evaluation. AJR Am J Roentgenol 2008; 190: 902-906.
17) Han BK, Lesser JR. CT imaging in congenital heart disease: an approach to imaging and interpreting complex lesions after surgical intervention for tetralogy of Fallot, transposition of the great arteries, and single ventricle heart disease. J Cardiovasc Comput Tomogr 2013; 7: 338-353.
18) Chan FP, Hanneman K. Computed tomography and magnetic resonance imaging in neonates with congenital cardiovascular disease. Semin Ultrasound CT MR 2015; 36: 146-160.
19) Sommer WH, Schenzle JC, Becker CR, Nikolaou K, Graser A, Michalski G, Neumaier K, Reiser MF, Johnson TR. Saving dose in triple-rule-out computed tomography examination using a high-pitch dual spiral technique. Invest Radiol 2010; 45: 64-71.
20) Sorensen C, Gach P, Pico H, Hugues N, Dabadie A, Desvignes C, Bourlière B, Aschero A, Colavolpe N, Petit P, Gorincour G. Cardiac CT or MRI in pediatric practice: which one to choose? Diagn Interv Imaging 2016; 97: 513-517.
21) Maceira AM, Prasad SK, Khan M, Pennell DJ. Reference right ventricular systolic and diastolic function normalized to age, gender and body surface area from steady-state free precession cardiovascular magnetic resonance. Eur Heart J 2006; 27: 2879-2888.
22) Helbing WA, de Roos A. Optimal imaging in assessment of right ventricular function in tetralogy of Fallot with pulmonary regurgitation. Am J Cardiol 1998; 82: 1561-1562.
23) Ammash NM, Dearani JA, Burkhart HM, Connolly HM. Pulmonary regurgitation after tetralogy of Fallot repair: clinical features, sequelae, and timing of pulmonary valve replacement. Congenit Heart Dis 2007; 2: 386-403.
24) Mooij CF, de Wit CJ, Graham DA, Powell AJ, Geva T. Reproducibility of MRI measurements of right ventricular size and function in patients with normal and dilated ventricles. J Magn Reson Imaging 2008; 28: 67-73.
25) Geva T. Indications for pulmonary valve replacement in repaired tetralogy of Fallot: the quest continues. Circulation 2013; 128: 1855-1857.
26) Knauth AL, Gauvreau K, Powell AJ, Landzberg MJ, Walsh EP, Lock JE, del Nido PJ, Geva T. Ventricular size and function assessed by cardiac MRI predict major adverse clinical outcomes late after tetralogy of Fallot repair. Heart 2008; 94: 211-216.

27) Therrien J, Provost Y, Merchant N, Williams W, Colman J, Webb G. Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. Am J Cardiol 2005; 95: 779-782.
28) Oosterhof T, van Straten A, Vliegen HW, Meijboom FJ, van Dijk AP, Spijkerboer AM, Bouma BJ, Zwinderman AH, Hazekamp MG, de Roos A, Mulder BJ. Preoperative thresholds for pulmonary valve replacement in patients with corrected tetralogy of Fallot using cardiovascular magnetic resonance. Circulation 2007; 116: 545-551.
29) Geva T. Repaired tetralogy of Fallot: the roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support. J Cardiovasc Magn Reson 2011; 13: 9.
30) Lee C, Kim YM, Lee CH, Kwak JG, Park CS, Song JY, Shim WS, Choi EY, Lee SY, Baek JS. Outcomes of pulmonary valve replacement in 170 patients with chronic pulmonary regurgitation after relief of right ventricular outflow tract obstruction: implications for optimal timing of pulmonary valve replacement. J Am Coll Cardiol 2012; 60: 1005-1014.
31) Bokma JP, Winter MM, Oosterhof T, Vliegen HW, van Dijk AP, Hazekamp MG, Koolbergen DR, Groenink M, Mulder BJ, Bouma BJ. Preoperative thresholds for mid-to-late haemodynamic and clinical outcomes after pulmonary valve replacement in tetralogy of Fallot. Eur Heart J 2016; 37: 829-835.
32) Alvarez-Fuente M, Garrido-Lestache E, Fernandez-Pineda L, Romera B, Sánchez I, Centella T, Abelleira C, Villagrá S, Tamariz R, Barrios E, Lamas MJ, Gomez R, Del Cerro MJ. Timing of pulmonary valve replacement: how much can the right ventricle dilate before it looses its remodeling potential? Pediatr Cardiol 2016; 37: 601-605.
33) Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, Khairy P, Landzberg MJ, Saidi A, Valente AM, Van Hare GF. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018; S0735-1097(18)36845-1.
34) Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, Crumb SR, Dearani JA, Fuller S, Gurvitz M, Khairy P, Landzberg MJ, Saidi A, Valente AM, Van Hare GF. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018; S0735-1097(18)36846-3.
35) Wijesekera VA, Raju R, Precious B, Berger AJ, Kiess MC, Leipsic JA, Grewal J. Sequential right and left ventricular assessment in post tetralogy of Fallot patients with significant pulmonary regurgitation. Congenit Heart Dis 2016; 11: 606-614.
36) Wald RM, Valente AM, Gauvreau K, Babu-Narayan SV, Assenza GE, Schreier J, Gatzoulis MA, Kilner PJ, Koyak Z, Mulder B, Powell AJ, Geva T. Cardiac magnetic resonance markers of progressive RV dilation and dysfunction after tetralogy of Fallot repair. Heart 2015; 101: 1724-1730.
37) Davlouros PA, Kilner PJ, Hornung TS, Li W, Francis JM, Moon JC, Smith GC, Tat T, Pennell DJ, Gatzoulis MA. Right ventricular function in adults with repaired tetralogy of Fallot assessed with cardiovascular magnetic resonance imaging: detrimental role of right ventricular outflow aneurysms or akinesia and adverse right-to-left ventricular interaction. J Am Coll Cardiol 2002; 40: 2044-2052.
38) Norton KI, Tong C, Glass RB, Nielsen JC. Cardiac MR imaging assessment following tetralogy of Fallot repair. Radiographics 2006; 26: 197-211.
39) Chang D, Kong X, Zhou X, Li S, Wang H. Unenhanced steady state free precession versus traditional MR imaging for congenital heart disease. Eur J Radiol 2013; 82: 1743-1748.
40) Hussain T, Lossnitzer D, Bellsham-Revell H, Valverde I, Beerbaum P, Razavi R, Bell AJ, Schaeffter T, Botnar RM, Uribe SA, Greil GF. Three-dimensional dual-phase whole-heart MR imaging: clinical implications for congenital heart disease. Radiology 2012; 263: 547-554.
41) Groth M, Henes FO, Bannas P, Muellerleile K, Adam G, Regier M. Intraindividual comparison of contrast-enhanced MRI and unenhanced SSFP sequences of stenotic and non-stenotic pulmonary artery diameters. Rofo 2011; 183: 47-53.
42) Winner MW, Raman SV, Chung YC, Simonetti OP, Mihai G, Cook SC. Post-interventional three-dimensional dark blood MRI in the adult with congenital heart disease. Int J Cardiol 2012; 158: 267-271.
43) Geva T, Greil GF, Marshall AC, Landzberg M, Powell AJ. Gadolinium-enhanced 3-dimensional magnetic resonance angiography of pulmonary blood supply in patients with complex pulmonary stenosis or atresia: comparison with x-ray angiography. Circulation 2002; 106: 473-478.
44) Groves EM, Bireley W, Dill K, Carroll TJ, Carr JC. Quantitative analysys of ecg-gated high-resolution contrast-enhanced MR angiography of the thoracic aorta. AJR Am J Roentgenol 2007; 188; 522-528.
45) Babu-Narayan SV, Kilner PJ, Li W, Moon JC, Goktekin O, Davlouros PA, Khan M, Ho SY, Pennell DJ, Gatzoulis MA. Ventricular fibrosis suggested by cardiovascular magnetic resonance in adults with repaired tetralogy of Fallot and its relationship to adverse markers of clinical outcome. Circulation 2006; 113: 405-413.
46) Miller CA, Naish JH, Bishop P, Coutts G, Clark D, Zhao S, Ray SG, Yonan N, Williams SG, Flett AS, Moon JC, Greiser A, Parker GJ, Schmitt M. Comprehensive validation of cardiovascular magnetic resonance techniques for the assessment of myocardial extracellular volume. Circ Cardiovasc Imaging 2013; 6: 373-383.
47) Kozak MF, Redington A, Yoo SJ, Seed M, Greiser A, Grosse-Wortmann L. Diffuse myocardial fibrosis following tetralogy of Fallot repair: a T1 mapping cardiac magnetic resonance study. Pediatr Radiol 2014; 44: 403-409.
48) Chen CA, Dusenbery SM, Valente AM, Powell AJ, Geva T. Myocardial ECV fraction assessed by CMR is associated with type of hemodynamic load and arrhythmia in repaired tetralogy of Fallot. JACC Cardiovasc Imaging 2016; 9: 1-10.

49) Hope MD, Meadows AK, Hope TA, Ordovas KG, Saloner D, Reddy GP, Alley MT, Higgins CB. Clinical evaluation of aortic coarctation with 4D flow MR imaging. J Magn Reson Imaging 2010; 31: 711-718.
50) Hope MD, Hope TA, Crook SE, Ordovas KG, Urbania TH, Alley MT, Higgins CB. 4D flow CMR in assessment of valve-related ascending aortic disease. JACC Cardiovasc Imaging 2011; 4: 781-787.
51) Kathiria NN, Higgins CB, Ordovas KG. Advances in MR imaging assessment of adults with congenital heart disease. Magn Reson Imaging Clin N Am 2015; 23: 35-40.
52) Geiger J, Markl M, Jung B, Grohmann J, Stiller B, Langer M, Arnold R. 4D-MR flow analysis in patients after repair for tetralogy of Fallot. Eur Radiol 2011; 21: 1651-1657.
53) François CJ, Srinivasan S, Schiebler ML, Reeder SB, Niespodzany E, Landgraf BR, Wieben O, Frydrychowicz A. 4D cardiovascular magnetic resonance velocity mapping of alterations of right heart flow patterns and main pulmonary artery hemodynamics in tetralogy of Fallot. J Cardiovasc Magn Reson 2012; 14: 16.
54) Chern MJ, Wu MT, Her SW. Numerical study for blood flow in pulmonary arteries after repair of tetralogy of Fallot. Comput Math Methods Med 2012; 2012: 198108.
55) Chern MJ, Wu MT, Wang HL. Numerical investigation of regurgitation phenomena in pulmonary arteries of tetralogy of Fallot patients after repair. J Biomech 2008; 41: 3002-3009.
56) Leonardi B, Taylor AM, Mansi T, Voigt I, Sermesant M, Pennec X, Ayache N, Boudjemline Y, Pongiglione G. Computational modelling of the right ventricle in repaired tetralogy of Fallot: can it provide insight into patient treatment? Eur Heart J Cardiovasc Imaging 2013; 14: 381-386.
57) Ordovas KG, Carlsson M, Lease KE, Foster E, Meadows AK, Martin AJ, Hope M, Do L, Higgins CB, Saeed M. Impaired regional left ventricular strain after repair of tetralogy of Fallot. J Magn Reson Imaging 2012; 35: 79-85.
58) Simpson SA, Field SL, Xu M, Saville BR, Parra DA, Soslow JH. Effect of weight extremes on ventricular volumes and myocardial strain in repaired tetralogy of Fallot as measured by CMR. Pediatr Cardiol 2018; 39: 575-584.
59) De Lorenzo A, Maiolo C, D'Agostino G, Arcudi G. Guidelines and malpractice in obesity treatment. Clin Ter 2006; 157: 143-52.
60) Merra G, Gratteri S, De Lorenzo A, Barrucco S, Perrone MA, Avolio E, Bernardini S, Marchetti M, Di Renzo L. Effects of very-low-calorie diet on body composition, metabolic state, and genes expression: a randomized double-blind placebo-controlled trial. Eur Rev Med Pharmacol Sci 2017; 21: 329-345.
61) Di Renzo L, Merra G, Botta R, Gualtieri P, Manzo A, Perrone MA, Mazza M, Cascapera S, De Lorenzo A. Post-prandial effects of hazelnut-enriched high fat meal on LDL oxidative status, oxidative and inflammatory gene expression of healthy subjects: a randomized trial. Eur Rev Med Pharmacol Sci 2017; 21: 1610-1626.
62) De Lorenzo A, Bernardini S, Gualtieri P, Cabibbo A, Perrone MA, Giambini I, Di Renzo L. Mediterranean meal versus Western meal effects on postprandial ox-LDL, oxidative and inflammatory gene expression in healthy subjects: a randomized controlled trial for nutrigenomic approach in cardiometabolic risk. Acta Diabetol 2017; 54: 141-149.
63) Ahmed S, Johnson PT, Fishman EK, Zimmerman SL. Role of multidetector CT in assessment of repaired tetralogy of Fallot. Radiographics 2013; 33: 1023-1036.
64) Lluri G, Aboulhosn JA, Moriarty JM, Finn JP, Ruehm SG, Budoff MJ, Vorobiof G, Yang EH. Applications of cardiac CT in the tetralogy of Fallot patient. JACC Cardiovasc Imaging 2014; 7: 1276-1279.
65) Perrone MA, Intorcia A, Morgagni R, Marchei M, Sergi D, Pugliese L, Ferrante P, Chiocchi M, Borzi M, Romeo F. Primary cardiac lymphoma: the role of multimodality imaging. J Cardiovasc Med (Hagerstown) 2018; 19: 455-458.
66) Dabizzi RP, Teodori G, Barletta GA, Caprioli G, Baldrighi G, Baldrighi V. Associated coronary and cardiac anomalies in the tetralogy of Fallot. An angiographic study. Eur Heart J 1990; 11: 692-704.
67) Young C, Taylor AM, Owens CM. Paediatric cardiac computed tomography: a review of imaging techniques and radiation dose consideration. Eur Radiol 2011; 21: 518-529.